

CLAIMS

1. Protein or peptide capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in figure 2.
2. Protein or peptide according to claim 1 wherein the cells are BLS 1 cell line or Na cell line or Ba cell line.
3. Protein or peptide according to claim 1 or 2 wherein the MHC-II is HLA-DR or HLA-DP or HLA-DQ.
4. Protein or peptide consisting or comprising the amino acid sequence shown in figure 2, an amino acid sequence having at least 80 % or preferably at least 90 % identity or similarity with the amino acid sequence shown in figure 2, a functional part of the amino acid sequence shown in figure 2 or a functional part of an amino acid sequence having at least 80 % and preferably at least 90 % homology with the amino acid sequence shown in figure 2.
5. Protein or peptide which is the homologous protein of a protein or a peptide of any one of claims 1 to 4 in another species than human.
6. Protein or peptide of claim 5 wherein the species is pig.
7. Antibodies capable of specifically recognising a peptide or protein according to any of claim 1 to 6.
8. Antibodies according to claim 7 which are monoclonal.
9. Antibodies according to claims 7 or 8 which are single chain antibodies.
10. Antibodies according to anyone of claims 7 to 9 which are capable of inhibiting a function or an activity of a protein or a peptide of any one of claims 1 to 6.

11. Nucleic acid molecule encoding a protein or a peptide according to any one of claims 1 to 6 or a chain of antibodies according to any one of claim 7 to 10.

12. Nucleic acid molecule according to claim 11 comprising all or part of the nucleotide sequence illustrated in figure 2.

13. Nucleic acid molecule comprising a sequence complementary to the nucleic acid molecules of any one of claims 11 to 12.

14. Nucleic acid molecule capable of hybridizing in stringent conditions, with the nucleic acid molecules of any one of claims 11 to 13.

15. Nucleic acid molecule comprising at least one of the sequences illustrated in figures 2, or a sequence exhibiting at least 90 % identity or similarity with any of these sequences, or a functional part of any one of these sequences.

16. Nucleic acid molecule of anyone of claims 11 to 15 comprises all or part of the DNA molecule encoding the RFXANK gene of a species other than human.

17. Nucleic acid molecule of claim 16 wherein the species is pig.

18. Nucleic acid molecule comprising a sequence complementary to the nucleic acid molecule of anyone of claims 11, 12 or 14 to 17.

19. Anti-sense molecule or ribozyme comprising a nucleic acid molecule of claim 13 or 18.

20. Vector comprising a nucleic acid molecule of any one of claims 11 to 19.

21. Process for identifying inhibitors which have the capacity to inhibit a function or an activity of a protein or a peptide according to any one of claims 1 to 6 or of a nucleic acid molecule according to any one of claims 11 to 18 comprising detecting or measuring of

said function or activity after intervention of the potential inhibitor.

22. Process according to claim 21 wherein said function or activity is the expression of MHC class II molecules.

23. Process according to claim 22 wherein the expression of MHC class II molecules is measured at the surface of cells.

24. Process according to claim 22 wherein the expression of MHC class II is measured at the mRNA level or in the cells.

25. Process according to claim 23 or 24 wherein said cells are B lymphocyte cell lines with constitutive expression of MHC class II or interferon gamma inducible cell lines.

26. Process according to claim 21 wherein said function or activity is the formation of RFX complex.

27. Process according to claim 21 wherein said function or activity is the binding of the RFX complex to its DNA target.

28. Process according to claim 27 wherein the measure or detection of the function or activity is done by gel retardation assay.

29. Process according to claim 21, wherein said function or activity is the interaction between the RFX complex and at least one of transcription factors X2BP, NF-Y and CIITA.

30. Process according to claim 21 wherein said function or activity is the correction of the MHC II expression defect of cell lines from complementation group B.

31. Process for identifying inhibitors which have the capacity to inhibit the synthesis of a protein or a peptide according to any one of claims 1 to 6 or of a nucleic acid molecule according to any one of claims 11 to 18 comprising detection or measuring a product which

contributes to the synthesis of said protein or peptide after intervention of the potential inhibitor.

32. Process according to claim 31 wherein said product is mRNA.

33. Process according to any one of claims 21 to 32 comprising a preliminary screening of said potential inhibitor which consists in screening for the binding of molecules to a peptide or a protein of any one of claims 1 to 6 or nucleic acid molecule of any one of claims 11 to 18.

34. Process of screening which consists in screening for the binding of molecules to a peptide or a protein of any one of claims 1 to 6 or a part thereof or which consists in screening for the binding of molecules to nucleic acid molecule of any one of claims 11 to 18 or a part thereof.

35. Process according to claim 33 or 34 wherein the binding of molecules is detected by ligand-induced charge in protein conformation.

36. Process according to claim 33 or 34 wherein the binding of molecules is detected by ligand-induced displacement of molecules first identified as binding to a peptide or a protein of any of claims 1 to 6.

37. Process for identifying inhibitors which have the capacity to inhibit a function, an activity or the synthesis of a protein or a peptide according to any one of claims 1 to 6 or of a nucleic acid molecule according to any one of claims 11 to 18 comprising the designing of said inhibitors on the basis of the three dimensional structure of a protein or a peptide according to any one of claims 1 to 6.

38. Process according to claim 37 wherein the three dimensional structure is obtained using X-Ray structure analysis or spectroscopic methods.

39. Process for identifying an inhibitor which has the capacity to inhibit recruitment of CIITA or to

inhibit the binding or fixation of CIITA to the MHC-class II enhanceosome, said process comprising the following steps :

- i) a DNA fragment consisting or comprising the W-X-X2-Y box region of the MHC II promoters is contacted with a mixture of cellular proteins comprising proteins binding to the W-X-X2-Y box region and CIITA, and with the substance to be tested ;
- ii) the thus formed DNA-protein complex is separated from the reaction mixture;
- iii) the presence or absence of CIITA in the proteins obtained after step ii) is detected, absence of CIITA indicating that the substance under test has a capacity to inhibit CIITA recruitment.

40. Process according to claim 39, wherein the DNA-protein complex is separated by fixation to a solid support able to purify said DNA-protein complex.

41. Process according to claim 40, wherein a solid support comprises magnetic beads or a microtitration plate.

42. Process according to any one of claim 41, wherein a DNA fragment consisting or comprising the W-X-X2-Y box region of the MHC II promoters is biotinylated.

43. Process according to any one of claim 39 to 42, wherein one or several wash(es) are carried out between step (ii) and step (iii) and/or wherein proteins binding DNA are separated from the DNA carried out between step (ii) and step (iii).

44. Process according to any one of claim 39 to 43, wherein the presence of CIITA in the proteins obtained after step iii) is detected by antibodies specific of CIITA.

45. Process according to any one of claim 39 to 44, wherein CIITA is chosen among : a recombinant or

recombinantly produced, a mutant CIITA, a mutant CIITA which has greater affinity for the MHC-class II enhanceosome than a wild-type CIITA, a truncated version of a wild-type CIITA.

46. Process according to any one of claims 39 to 45, wherein CIITA is tagged or wherein CIITA comprises a Fluorescent Protein or an epitope.

47. Process according to any one of claims 39 to 46, wherein the substances to be tested are CIITA dominant negative mutants.

48. Process according to any one of claims 39 to 47, wherein the mixture of cellular proteins and CIITA comprises a nuclear extract of CIITA+ cells.

49. Process according to any one of claims 39 to 48 further comprising a step of separating the proteins bound to the DNA from the DNA and optionally detecting the presence or absence of any of the proteins capable of binding to the W-X-X2-Y region of the MHC-class II promoters, the absence of any of these proteins indicating that the substance under test is capable of inhibiting the binding of said protein to DNA.

50. Inhibitor identifiable by a process according to any one of claims 21 to 49.

51. Inhibitor according to claim 50 which is an antibody according to any one of claims 7 to 8, a nucleic acid molecule according to claim 13 or 18 a derivative of a protein or a peptide according to any one of claims 1 to 6 or of a nucleic acid molecule according to any one of claims 11 to 18, or an anti-sense molecule or a ribozyme according to claim 19.

52. Inhibitor according to claim 50 which is an antibody, a single chain antibody, a dominant negative mutant, a protein, a peptide, a small molecular weight molecule, a ribozyme or an anti-sense molecule.

53. Inhibitors of a protein or a peptide according to any one of claims 1 to 6, or of a nucleic acid molecule according to any one of claims 11 to 18.

54. Nucleic acid molecule encoding an inhibitor of any one of claims 50 to 53.

55. Inhibitor according to any one of claims 50 to 54 for use in therapy.

56. Pharmaceutical composition comprising an inhibitor according to any one of claims 50 to 54, optionally in association with a pharmaceutically acceptable vehicle.

57. Use of an inhibitor according to any one of claims 50 to 54 for the preparation of a medicament for use in therapy or prevention of diseases associated with aberrant expression of MHC class II genes.

58. Use of an inhibitor according to any one of claims 50 to 54 as an immunosuppressive agent.

59. Protein complex comprising cellular proteins capable of binding to the W-X-X2-Y box of MHC-class II promoters and CIITA.

60. Protein complex according to claim 59 wherein CIITA is : a recombinant or recombinantly produced CIITA, a mutant CIITA, a mutant CIITA which has greater affinity for the MHC-class II enhanceosome than a wild-type CIITA or a truncated version of a wild-type CIITA.

61. Antibodies capable of specifically recognizing a protein complex according to claims 59 and 60.